

In re Application of:
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Attorney Docket No.: JHU1470-3

I. CLAIMS

Please add new claims 46 to 58, and amend the claims as indicated below. Upon entry of the present amendment, the status of the claims will be as follows:

1. (Currently amended) A transgenic non-human mammal whose genome contains a nucleic acid sequence comprising a truncated Activin Type II receptor gene, which encodes a truncated dominant negative Activin Type II receptor lacking kinase activity, and a regulatory element comprising a muscle-specific promoter operably linked and integrated into the genome of the transgenic mammal, wherein the nucleic acid sequence is expressed so as to result in elevated levels of the truncated Activin Type II receptor and increased muscle mass in the transgenic mammal as compared to a corresponding nontransgenic mammal.
2. (Currently amended) The transgenic mammal of claim 1, wherein the ~~muscle-specific promoter is regulatory element comprises~~ a myosin light chain ~~promoter/enhancer~~ promoter and an enhancer.
3. (Previously presented) The transgenic mammal of claim 1, wherein the Activin Type II receptor is an Activin RIIA or an Activin RIIB.
4. (Cancelled)
5. (Previously presented) The transgenic mammal of claim 1, wherein the truncated Activin RIIB comprises amino acid residues 1-174 of Activin RIIB.
- 6 to 12. (Cancelled)

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13. (Currently amended) An expression cassette comprising a DNA segment ~~encoding~~ comprising a truncated dominant negative Activin RIIB receptor ~~gene~~ operably linked to a regulatory element comprising a muscle-specific control sequence promoter.

14. (Currently amended) The expression cassette of claim 13 wherein the ~~muscle-specific promoter is~~ regulatory element comprises a myosin light chain ~~promoter/enhancer~~ promoter and an enhancer.

15 to 19. (Cancelled)

20. (Currently amended) A cell or cell line isolated from the transgenic mammal of claim 1, wherein said cell expresses the truncated dominant negative Activin Type II receptor.

21 to 39. (Cancelled)

40. (Currently amended) A method of producing a chimeric non-human mammal, the method comprising:

obtaining an ovum from ovaries of a non-human mammal;
maturing the ovum *in vitro*;
fertilizing the mature ovum *in vitro* to form a zygote;
introducing into the zygote *in vitro* a nucleic acid construct comprising in operable association a DNA sequence encoding a truncated dominant negative Activin Type II receptor, which lacks kinase activity, and a regulatory sequence element comprising a muscle-specific promoter that promotes expression of the DNA sequence encoding the truncated dominant negative Activin Type II receptor;
maturing the zygote to a preimplantation stage embryo *in vitro*; and

transplanting the embryo into a recipient female mammal of the same species, wherein the female mammal gestates the embryo to produce a chimeric animal.

41. (Currently amended) A method of producing food products from a transgenic non-human mammal having increased muscle mass comprising:

- a) introducing a transgene comprising in operable association a DNA sequence encoding a truncated dominant negative Activin Type II receptor, which lacks kinase activity, and a regulatory element comprising a muscle-specific promoter into germ cells of a pronuclear embryo of the mammal;
- b) implanting the embryo into the oviduct of a pseudopregnant female of the same species, thereby allowing the embryo to mature to full term progeny;
- c) testing the progeny for presence of the transgene to identify transgene-positive progeny;
- d) cross-breeding transgene-positive progeny to obtain further transgene-positive progeny; and
- e) processing the progeny to obtain food products.

42. (Currently amended) A method of producing food products from a transgenic ovine, porcine, or bovine mammal having increased muscle mass comprising:

- a) introducing a transgene comprising in operable association a DNA sequence encoding a truncated dominant negative Activin Type II receptor, which lacks kinase activity, and a regulatory element comprising a muscle-specific promoter into an embryo of an ovine, porcine, or bovine mammal;
- b) implanting the embryo into the oviduct of a pseudopregnant female of the same species, thereby allowing the embryo to mature to full term progeny;

- c) testing the progeny for presence of the transgene to identify transgene-positive progeny;
- d) cross-breeding transgene-positive progeny to obtain a transgenic ovine, porcine, or bovine mammal; and
- e) processing the transgenic mammal to obtain food products.

43. (Previously presented) The transgenic non-human mammal of claim 1, wherein the mammal is ovine, porcine, or bovine.

44. (Previously presented) The chimeric non-human mammal of claim 40, wherein the mammal is ovine, porcine, or bovine.

45. (Previously presented) The transgenic non-human mammal of claim 41, wherein the mammal is ovine, porcine, or bovine.

46. (New) The method of claim 1, wherein the regulatory element comprises a myosin light chain promoter and 1/3 enhancer.

47. (New) The expression cassette of claim 13, wherein the regulatory element comprises a myosin light chain promoter and 1/3 enhancer.

48. (New) A transgenic non-human mammal whose genome contains a nucleic acid sequence comprising a truncated Activin Type II receptor gene, which encodes a truncated dominant negative Activin Type II receptor lacking kinase activity, and a myosin light chain promoter and 1/3 enhancer operably linked and integrated into the genome of the transgenic mammal, wherein the nucleic acid sequence is expressed so as to result in elevated levels of the

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truncated dominant negative Activin Type II receptor and increased muscle mass in the transgenic mammal as compared to a corresponding nontransgenic mammal.

49. (New) The transgenic mammal of claim 48, wherein the Activin Type II receptor is an Activin RIIA or an Activin RIIB.

50. (New) The transgenic mammal of claim 48, wherein the truncated Activin RIIB comprises amino acid residues 1-174 of Activin RIIB.

51. (New) The transgenic non-human mammal of claim 48, wherein the mammal is ovine, porcine, or bovine.

52. (New) A cell or cell line isolated from the transgenic mammal of claim 48, wherein said cell expresses the truncated dominant negative Activin Type II receptor.

53. (New) An expression cassette comprising a DNA segment encoding a truncated dominant negative Activin RIIB receptor operably linked to a myosin light chain promoter and 1/3 enhancer.

54. (New) A method of producing a chimeric non-human mammal, the method comprising:

obtaining an ovum from ovaries of a non-human mammal;
maturing the ovum *in vitro*;
fertilizing the mature ovum *in vitro* to form a zygote;
introducing into the zygote *in vitro* a nucleic acid construct comprising in operable association a DNA sequence encoding a truncated dominant negative Activin

Type II receptor, which lacks kinase activity, and a myosin light chain promoter and 1/3 enhancer, which promotes expression of the DNA sequence encoding the truncated dominant negative Activin Type II receptor;

maturing the zygote to a preimplantation stage embryo *in vitro*; and
transplanting the embryo into a recipient female mammal of the same species,
wherein the female mammal gestates the embryo to produce a chimeric animal.

55. (New) The chimeric non-human mammal of claim 52, wherein the mammal is ovine, porcine, or bovine.

56. (New) A method of producing food products from a transgenic non-human mammal having increased muscle mass comprising:

- a) introducing a transgene comprising in operable associate a DNA sequence encoding a truncated dominant negative Activin Type II receptor, which lacks kinase activity, and a myosin light chain promoter and 1/3 enhancer, into germ cells of a pronuclear embryo of the mammal;
- b) implanting the embryo into the oviduct of a pseudopregnant female of the same species, thereby allowing the embryo to mature to full term progeny;
- c) testing the progeny for presence of the transgene to identify transgene-positive progeny;
- d) cross-breeding transgene-positive progeny to obtain further transgene-positive progeny; and
- e) processing the progeny to obtain food products.

57. (New) The method of claim 56, wherein the mammal is ovine, porcine, or bovine.

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58. (New) A method of producing food products from a transgenic ovine, porcine, or bovine mammal having increased muscle mass comprising:

- a) introducing a transgene comprising in operable associate a DNA sequence encoding a truncated dominant negative Activin Type II receptor, which lacks kinase activity, and a myosin light chain promoter and 1/3 enhancer into an embryo of an ovine, porcine, or bovine mammal;
- b) implanting the embryo into the oviduct of a pseudopregnant female of the same species, thereby allowing the embryo to mature to full term progeny;
- c) testing the progeny for presence of the transgene to identify transgene-positive progeny;
- d) cross-breeding transgene-positive progeny to obtain a transgenic ovine, porcine, or bovine mammal; and
- e) processing the transgenic mammal to obtain food products.